IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (JLH) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff/Counter Defendants.	[redacted] [redacted] REDACTED - PUBLIC VERSION

NS'S RESPONSE TO SAREPTA THERAPEUTICS, INC. AND THE UNIVERSITY OF WESTERN AUSTRALIA'S MOTIONS TO EXCLUDE EXPERT OPINION AND TESTIMONY

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I. INTRODUCTION

Defendants-Counterclaim Plaintiffs Sarepta Therapeutics, Inc. and the University of Western Australia (together, "Sarepta") seek to exclude opinions and testimony of NS's experts Michelle L. Hastings and Matthew JA Wood, including several bases of exclusion that could have been raised before. Pursuant to this Court's scheduling order, D.I. 597, any *Daubert* motions were to be "limited to Supplemental Technical Expert Reports and the related Technical Expert Depositions." Sarepta's motions are not so limited and should be denied on that basis alone.

Even if the motions are considered on the merits, they must fail.

First, Sarepta seeks to exclude the testimony of Dr. Hastings and Dr. Wood for allegedly using a new and incorrect construction of the term "morpholino." There is a dispute over the plain and ordinary meaning of that the term, but its impact is limited. Dr. Hastings and Dr. Wood expressly did not rely on the broader (and correct) meaning of "morpholino" in reaching their opinions. Sarepta seizes on the parties' disagreement to seek broad exclusion of any testimony about the scope of the claims and Sarepta's own prior statements and arguments to the Patent Office. The Court should reject Sarepta's overreach in its Motion #1.

Second, Sarepta seeks to exclude *all* of Dr. Wood's proposed opinions and testimony as "irrelevant and unhelpful," including reaching back to Dr. Wood's October 2023 opinions rebutting Sarepta's arguments that NS's patents are invalid. But Dr. Wood's opinions as to Sarepta's '851 patent center on interpreting the specification from the perspective of a POSA—a topic that is directly relevant to NS's written description challenge. Sarepta previously conceded that Dr. Wood's "[f]indings regarding what a POSA would have recognized or understood the inventors to have invented are [] pertinent to evaluating written description." D.I. 389 at 1-2. And Sarepta's other inventorship challenge is just a repackaging of Sarepta's previous and unsuccessful motion to exclude "state of mind" opinions. *See* D.I. 393, 395, 553. The Court need not reconsider

the issues raised in Motion #2 because Sarepta has violated this Court's scheduling order, but if it does, the Court should deny the motion.

Third, Sarepta seeks to exclude Dr. Hastings' opinions about enablement of 5' and 3' end modifications despite Sarepta's admission that "such modifications are **not excluded** from the claim." D.I. 611 at 13 (emphasis added). Both Federal Circuit and this Court's precedent dictate that a patentee must enable the **full scope** of the claim. The cases on which Sarepta relies to argue otherwise are either explicitly not on point or are so old as to predate modern enablement law. The Court should deny Motion #3.

Fourth, Sarepta seeks to exclude Dr. Hastings' opinions because she discusses extrinsic evidence in her written description analysis. But there is nothing per se improper in an expert considering extrinsic evidence so long as her opinions are "tethered to" the patent specification—which Dr. Hastings' opinions are here. Sarepta also mischaracterizes written description law in arguing that a description of one narrow embodiment is always enough to support an entire broad claimed genus. This contradicts Federal Circuit guidance warning against allowing an inventor to claim a scope far greater than what a POSA would understand the inventor to possess. Sarepta may disagree with Dr. Hastings' opinions on claim scope and written description sufficiency, but the proper way to address that is via its own witnesses and via cross-examination. Motion #4 fails as well.

II. ARGUMENT IN RESPONSE TO MOTION #1

The '851 patent does not define the term "morpholino." The sole reference to "morpholino" in the specification is found in the header of Table 1A, which states "[w]ith other antisense chemistries such as… morpholinos, these U bases may be shown as 'T'." D.I. 2-9, Ex. I ('851 patent), Col. 7. Sarepta seeks to limit the generic term "morpholino" to a specific type of morpholino oligomer, namely one with phosphorodiamidate intersubunit linkages. This type of

morpholino is often abbreviated as "PMO" for **p**hosphorodiamidate **m**orpholino **o**ligomer. D.I. 612, Ex. 1, ¶ 55. Contrary to Sarepta's assertion, NS neither offered nor accepted a narrower construction because "morpholino" was not previously disputed. *See* D.I. 144-2. The term has not been construed by the Court, and, therefore, its plain and ordinary meaning applies. The evidence shows that the plain and ordinary meaning of "morpholino" to a person of ordinary skill in the art as of June 2005 was broader than just the PMO sub-type. And, even if the Court holds otherwise that would not warrant the broad exclusion Sarepta seeks in its Motion #1.

A. The Evidence Shows that "Morpholino" is a Generic Term

James A. Summerton and Dwight Weller developed the morpholino antisense chemistry. *See* D.I. 612, Ex. 2 ("Summerton 1997"). During prosecution of the '851 patent, the applicants cited Summerton 1997 and two other articles as evidence that "[m]orpholino antisense oligonucleotides have been described in the literature." D.I. 612, Ex. 15 at DTX-0004-118. Sarepta relies on these three articles as confirming "that a POSA would understand 'morpholino' to refer to PMOs." D.I. 611 at 8. However, Dr. Wood and Dr. Hastings have opined that Summerton 1997 in fact illustrates that the plain, ordinary, and scientifically precise meaning of "morpholino" refers to compounds with a morpholino ring, of which PMO is but one type. Ex. 1 (Wood Suppl. Tr.) 30:24-31:8, 121:2-5; D.I. 612, Ex. 3 (Hastings Suppl. Tr.) 110:14-25.

As shown in Fig. 3 of Summerton 1997, to make a "Morpholino subunit," the ribose moiety of a ribonucleoside (on the left) is converted via a sequence of chemical reactions to a morpholine moiety (on the right), which gives "morpholinos" their name (D.I. 612, Ex. 2 at DTX-0542-8):

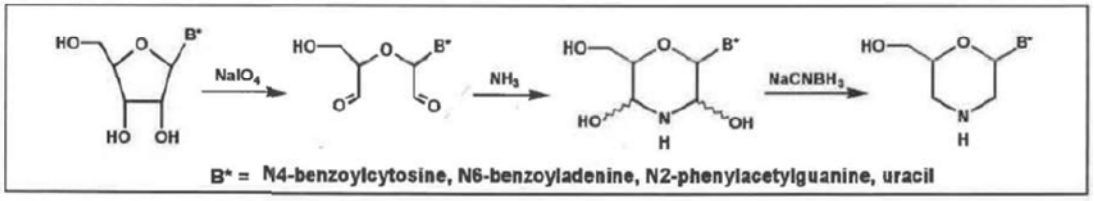

FIG. 3. Conversion of ribonucleoside to Morpholino subunit.

Summerton 1997 goes on to describe how different linkages (annotated) joining the morpholino subunits were assessed (*id.* at DTX-0542-9; *see also* D.I. 612, Ex. 7 at ¶¶ 83-85):

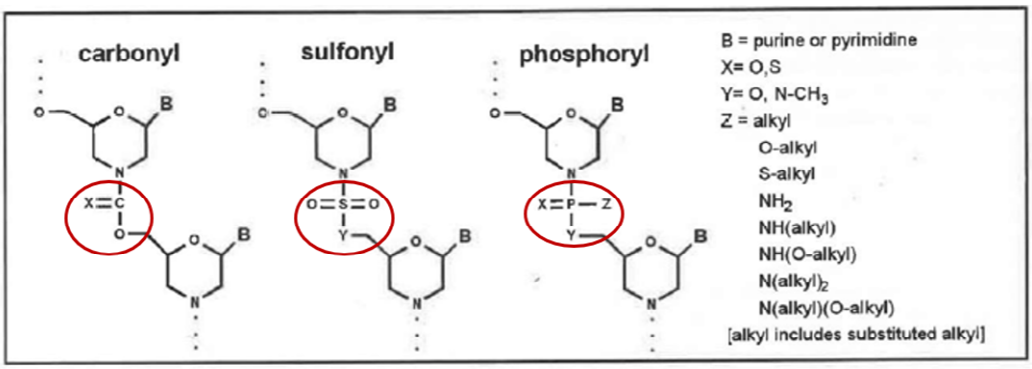

FIG. 4. Intersubunit linkage types for Morpholino oligos.

A PMO is an even more specific structure than the "phosphoryl" linkage shown generically above in Summerton 1997 Fig. 4. In a PMO, the -X and -Z groups of the phosphoryl linkage are oxygen and diamidate ($N(CH_3)_2$), respectively (D.I. 612, Ex. 2 at DTX-0542-7 (annotated):

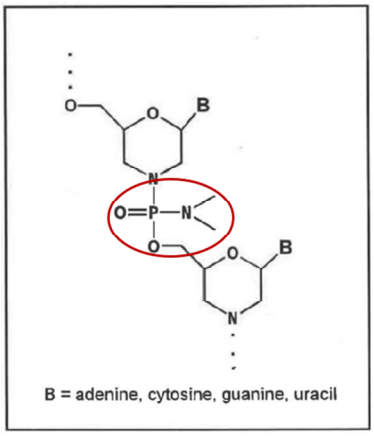

FIG. 2. Morpholino oligo structure.

Sarepta argues that Fig. 2 purports to define the structure of "morpholino." D.I. 611 at 7. However, Summerton 1997 introduces Fig. 2 as "a novel Morpholino structural type (Fig. 2)" and only later notes that the authors "focus[ed] on the phosphorodiamidate shown in Figure 2 as our principle linkage type." D.I. 612, Ex. 2 at DTX-0542-7, 8. Summerton 1997 then discusses properties of such "phosphorodiamidate-linked Morpholino oligos" and methods for assembling "phosphorodiamidate-linked Morpholino oligos." *Id.* at DTX-0542-8. Thus, Summerton 1997

distinguishes between "morpholino" and "phosphorodiamidate-linked morpholinos." This supports NS's position, not Sarepta's. D.I. 612, Ex. 3 (Hastings Suppl. Tr.) at 74:6-75:11. Sarepta's reliance on the other two articles cited to the USPTO is similarly unavailing because they both cite back to Summerton 1997. D.I. 612, Ex 17 at ¶ 19, Ex. 13 at SRPT-VYDS-0247376, Ex. 14 at DTX-0429-2.

Sarepta's prosecution of the related U.S. 9,024,007 patent further supports a broader plain and ordinary meaning of "morpholino." *See* D.I. 611 at 7. There, applicants characterized Hudziak et al., US 20030166588, as art "consistent with the established meaning" of "morpholino antisense oligonucleotide." D.I. 612, Ex. 10 at SRPT-VYDS-0247402. Hudziak issued as U.S. Patent No. 6,784,291 and is assigned to Sarepta's predecessor AVI BioPharma, Inc. D.I. 612, Ex. 8. The '291 patent **defines** "morpholino oligomer" as encompassing multiple intersubunit "linkages shown in Figs. 2A-A to 2E-E," consistent with Dr. Hastings' and Dr. Wood's opinions. *Id.* at 3:56-66. Other Sarepta patents define "morpholino" similarly broadly. *See* D.I. 612, Ex. 4 at ¶ 62. Hudziak then goes on to state that "a preferred morpholino oligonucleotide" is shown in Fig. 2B-B "where the structures are linked together by phosphorodiamidate linkages." D.I. 612, Ex. 8 at Col. 4:8-11. Hudziak also specifies that a "PMO" is the structure shown in Fig. 2B-B where the Y_1 and Z are oxygen and X is $N(CH_3)_2$, which is again consistent with Dr. Hastings' and Dr. Wood's opinions. *Id.* at Col. 9:1-2.

As Dr. Wood and Hastings have acknowledged, "morpholino" is often used interchangeably with "PMO." D.I. 612, Ex. 4 at ¶ 61 and Ex. 7 at ¶ 82. "Often" is not "always," however, and Dr. Wood's Interference declaration and Dr. Hastings' claim construction declaration both clarify that they are electing to use the terms morpholino and PMOs interchangeably—reflecting that interchangeability is not implicit nor automatic. D.I. 612, Ex. 1

at ¶¶ 52, 55; D.I. 171, Ex. 43 at ¶ 110. Similarly, in the Aartsma-Rus 2004 article cited by Sarepta, the authors first use the more precise term "morpholino-phosphorodiamidate" and then note that they call them "morpholinos." D.I. 612, Ex. 11 at NS00157155.

In sum, despite Sarepta's arguments to the contrary, the evidence supports that the plain and ordinary meaning of "morpholino" includes multiple types of intersubunit linkages and is not limited to PMOs.

B. Sarepta Grossly Overreaches in Its Requested Relief

While there is a dispute over the meaning of the term "morpholino," that dispute is relatively narrow. If the Court were to adopt the narrower definition, it would only affect a small subset of Dr. Hastings' and Dr. Wood's opinions. Yet Sarepta uses this narrow dispute as a pretext to seek far broader exclusions of their opinions. The paragraphs of Dr. Hastings' and Dr. Wood's expert reports that Sarepta seeks to exclude (D.I. 607 at 1-2) are discussed below.

Dr. Hastings' Supplemental Expert Report (D.I. 612, Ex. 4):

- Paragraphs 81, 83, 184, 203, 214-217 reference calculations that ***expressly omitted*** possible variations in intersubunit linkages. *See* D.I. 612 Ex. 4 at ¶¶ 75-76 ("These options [for modified bases and chemical moieties] ***alone*** show that at least tens of thousands of ASOs meet all of the claims' structural limitation [sic].") and ¶ 80 ("my calculations above ***did not account*** for possible variations in inter-nucleotide linkages") (emphasis added).

- Paragraph 104 quotes arguments that Sarepta itself made to the USPTO in Interference No. 106,007 that merely mention internucleotide linkages in passing.

- Paragraphs 123-124, 126 do not concern intersubunit linkages at all, but rather discusses what the patent specification does and does not disclose, and expresses a general opinion on its failure to disclose a common structural feature for the genus.

- Paragraphs 194-195, 206-207, and 214-217 discuss publications on and experiments with PMOs and are therefore consistent with Sarepta's proposed interpretation of "morpholino" as "PMO."

Of the paragraphs Sarepta seeks to strike, only paragraphs 61-64, part of the conclusion in paragraph 65, and the first sentence of paragraph 200 of Dr. Hastings' Supplemental Report discuss alternative intersubunit linkages.

Dr. Hastings' Supplemental Reply Report (D.I. 612, Ex. 17):

- Paragraphs 13-16 and 111 discuss calculations of the size of the genus that expressly excluded variations in intersubunit linkages. *See* D.I. 612 Ex. 17 at ¶ 13 and n.2 (reiterating that the estimated "number of chemically-distinct ASO candidates… ***do[es] not account*** for variations in intersubunit linkages") (emphasis added).

- Paragraphs 49, 91, 93 and 117 do not concern intersubunit linkages at all but rather discuss modified bases and end modifications that Sarepta agrees are encompassed by the claims. D.I. 611 at 13.

- Paragraphs 79, 85, 91, 93 and 119 express general conclusions that are not premised on variations in intersubunit linkages.

Of the paragraphs Sarepta seeks to exclude, only paragraphs 18-21 of Dr. Hastings' Supplemental Reply Report discuss alternative intersubunit linkages.

Dr. Wood's Supplemental Report (D.I. 612, Ex. 7). Paragraphs 27-28 discuss PMOs and are thus consistent with Sarepta's interpretation of the claims, and paragraph 77 discusses disclosures in the patent specification. Of the paragraphs Sarepta seeks to exclude, only paragraphs 82-86 of Dr. Wood's Supplemental Report discuss alternative intersubunit linkages.

Dr. Wood's Supplemental Reply Report (D.I. 612, Ex. 6). Sarepta seeks to exclude paragraph 14, which provides nearly four full pages of direct quotes from his two Interference Declarations that are party admissions applicable to this litigation and have nothing to do with alternative intersubunit linkages. Paragraphs 65 and 82 discuss PMOs and are thus consistent with Sarepta's interpretation of "morpholino" as "PMO." Of the paragraphs Sarepta seeks to strike, only paragraph 60 of Dr. Wood's Supplemental Reply Report discusses alternative intersubunit linkages.

* * *

The Court should deny Sarepta's Motion #1 because Sarepta is improperly raising a claim construction dispute in its *Daubert* motion, and, in any event, Sarepta's proposed construction is unduly narrow. If the Court were to grant any relief, it should be limited to only the opinions and testimony directly based on a broader interpretation of "morpholino," namely, only paragraphs 61-64, a portion of paragraph 65, and the first sentence of paragraph 200 of Dr. Hastings' Supplemental Report; paragraphs 18-21 of Dr. Hastings' Supplemental Reply Report; paragraphs 82-86 of Dr. Wood's Supplemental Report; and paragraph 60 of Dr. Wood's Supplemental Reply Report.

III. ARGUMENT IN RESPONSE TO MOTION #2

Sarepta is desperate to exclude Dr. Wood as reflected by its multiple attempts to exclude or strike Dr. Wood or his opinions. *See* D.I. 220, 298, 299, 308, 309, 313, 321, 384, 385, 389, 393, 395, 458, 459, 517; *see also* D.I. 594. The Court has previously rejected them all. D.I. 543, 553. Sarepta then acquiesced to Dr. Wood testifying about the '851 patent. *See* D.I. 570 (Pre-Trial Conf. Tr.) 39:6-7 (Sarepta's counsel arguing "we think [Dr. Wood] should be limited to offering testimony about the [UWA] patents-in-suit").

In its latest attempt to exclude Dr. Wood, Sarepta characterizes his proposed opinions and testimony as "irrelevant and unhelpful," and argues it will confuse the jury. However, Sarepta's current characterization of Dr. Wood's testimony as irrelevant directly contradicts its prior representations to this Court that Dr. Wood's opinions "directly address[] NS's defense that the Wilton Patents are invalid under 35 U.S.C. § 112, including what a person of ordinary skill in the art ('POSA') would have understood the Wilton Patent inventors to have invented" and that "[f]indings regarding what a POSA would have recognized or understood the inventors to have

invented are thus pertinent to evaluating written description." D.I. 389 at 1-2. Sarepta makes no attempt to reconcile its inconsistent arguments to this Court.

Dr. Wood's opinions are relevant to both sides' patents.[1] With respect Sarepta's asserted patent, they center on interpreting the '851 patent from the perspective of a POSA—a topic that is directly relevant to NS's lack of written description arguments. *See, e.g.*, *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) ("the [written] description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."); *Synthes USA, LLC v. Spinal Kinetics, Inc.*, 734 F.3d 1332, 1341 (Fed. Cir. 2013) ("Section 112, paragraph one of Title 35 requires a patentee to provide a written description that allows a person of skill in the art to recognize that the patentee invented what is claimed."); *accord ICU Med., Inc. v. Alaris Med. Sys., Inc.*, 558 F.3d 1368, 1378 (Fed. Cir. 2009) (holding claims invalid under § 112 where "a person of skill in the art would not understand the inventor . . . to have invented" the claimed invention). With respect to NS's patents, relevant topics addressed by Dr. Wood include unpredictability of exon skipping, and whether the '851 patent or any of Dr. Wilton's publications identified a "hot spot" as Sarepta claims. *See, e.g.*, D.I. 427-1 (Dowdy Opening) ¶¶ 101-102, 110; Ex. 2 (Wood Rebuttal) ¶¶ 11, 65-69.

Indeed, Dr. Wood's testimony will be particularly helpful to the fact-finder. Dr. Wood is the only expert in this litigation who was working in the field of developing exon skipping ASOs to treat Duchenne Muscular Dystrophy as of the priority dates of both sides' patents. Sarepta's expert Dr. Dowdy was not working in the field as of June 2005. D.I. 612, Ex. 6 (Wood Suppl.

[1] Without argument or explanation, Sarepta seeks to exclude opinions and testimony Dr. Wood has offered in his October 11, 2023 report responding to Sarepta's arguments that **NS's patents** are invalid. The Court previously rejected a similar request, and it should do so again. *See* D.I. 384; D.I. 553.

Reply) at ¶ 6. NS's expert Dr. Hastings works in the splice-switching antisense oligonucleotide field, but not specifically on DMD treatments. Ex. 3 (Hastings Suppl. Tr.) at 9:14-10:7. Dr. Wood is uniquely situated in terms of his specific expertise and first-hand knowledge of the field. His testimony will help the jury understand the state of the art of exon skipping therapies at the relevant time frames.

Sarepta implies that Dr. Wood did not apply the legally relevant time frame for assessing the state of the art in his supplemental reports. D.I. 611 at 10. However, Dr. Wood's supplemental reports are replete with references to the relevant time frame: the June 2005 priority date of the '851 patent. *See, e.g.*, D.I. 612, Ex. 7 (Wood Suppl.) at 2, 12, 15-17. Similarly, Dr. Wood's supplemental reports and testimony refute Sarepta's assertion (D.I. 611 at 10-11) that Dr. Wood is offering subjective opinions rather than objective ones. Dr. Wood's reports make clear that he is offering "testimony about the state of the art and what persons of ordinary skill in the art thought about the inventors' work at the time"—topics Sarepta concedes are relevant, D.I. 611 at 11—as well as highly probative testimony about the general skill, knowledge, and capabilities of scientists working in the field of exon skipping. *See* D.I. 612, Ex. 7 (Wood Suppl.) ¶¶ 29-44, 53-60.

The fact that Dr. Wood does not offer an opinion on the ultimate issue of validity is of no consequence. Previously courts strictly prohibited experts from opining on the "ultimate issue." *See* Advisory Committee Notes to Fed. R. Evid. 704. However, the rule was amended because it proved to be "unduly restrictive" of experts. *Id.* But the amendment did not create a requirement to opine on the ultimate issue, nor did it indicate that failure to do so would confuse the jury. Rather, the proper test is simply whether an expert's opinion will be helpful to the jury. *See* Advisory Committee Notes to Fed. R. Evid. 704 ("The basic approach to opinions, lay and expert, in these rules is to admit them when helpful to the trier of fact."). Sarepta said it best: "Dr. Wood's

opinions . . . directly concern the validity of the Wilton Patents," so they will be helpful to the trier of fact. D.I. 389 at 1-2.

Next, Sarepta challenges Dr. Wood's purported opinions on inventorship. D.I. 611 at 10-11. But Sarepta's argument centers on what Dr. Wood opined that the inventors and POSAs would "recognize and appreciate." *Id.* This is exactly what is required under the written description standard. *See Synthes USA*, 734 F.3d at 1341. Further, Sarepta's arguments are ***identical*** to arguments it made in a previous and unsuccessful motion to exclude "state of mind" opinions. *See* D.I. 393 at 13-14, 395 and 489 at 6-7 (Sarepta's previous *Daubert* filings); D.I. 553 (denying Sarepta's motion because "[t]he Court is unpersuaded that Section V of Dr. Wood's Opening Report and Section II of his Reply Report amount to improper opinions about the inventors' states of mind"). Sarepta is not presenting any new arguments for why Dr. Wood's opinions should be excluded, illustrating that its motion is not "limited to Supplemental Technical Expert Reports and the related Technical Expert Depositions," as the Court's scheduling order required. D.I. 597. And in any event, as noted above, how a POSA would interpret the '851 patent and what a POSA would understand to be disclosed is relevant and helpful to the jury.

Next, Sarepta challenges Dr. Wood's opinions and testimony as "needlessly cumulative to and improperly bolstering of Dr. Hasting's proposed opinions and testimony." D.I. 12. The opinions are not cumulative, as the experts rely on different sources of proof and interpret the evidence in different ways. For example, Dr. Hastings focuses on analyzing the patent's specification in view of [redacted] that Dr. Wood was prohibited from seeing under the Protective Order. Dr. Wood instead primarily focused on publicly available documents. In any event, that one expert's testimony may be "somewhat duplicative of" another "is not a basis for excluding his testimony since the trial will be timed and the parties will not be

given time to waste." *St. Clair Intell. Prop. Consultants, Inc. v. Acer, Inc.*, 935 F. Supp. 2d 779, 781 (D. Del. 2013); *see also Sanofi v. Glenmark Pharm. Inc., USA*, 2016 WL 10957311, at *2 (D. Del. May 12, 2016) ("A considerable portion of Defendants' argument is simply that Dr. Thisted's testimony will be cumulative of testimony from Dr. Reiffel . . . . This does not provide grounds for exclusion under *Daubert*."). NS will have only 11 hours to present its entire offensive and defensive case, so it will be motivated to avoid presenting duplicative expert testimony. NS should not be prevented from trying its case in the manner of its choosing.

Finally, while expert testimony that serves **solely** to bolster the credibility of another expert may be improper, there is nothing wrong in NS introducing testimony where, as is the case here, the expert offers his own methodology and independent analysis. *Cf. Roche Diagnostics Corp. v. Meso Scale Diagnostics, LLC*, 2019 WL 5310220, at *3 (D. Del. Oct. 21, 2019) ("The Court will exclude Dr. Crooks' testimony because it serves no purpose beyond improperly attempting to bolster the opinions of another expert, i.e., Dr. Leventis. Dr. Crooks does not seek to offer his own methodology or independent analysis.").

This motion should be denied.

IV. ARGUMENT IN RESPONSE TO MOTION #3

Enablement requires that "the specification teach those in the art to make and use the invention without undue experimentation." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). A claim is not enabled when, "at the effective filing date of the patent, one of ordinary skill in the art could not practice their ***full scope*** without undue experimentation." *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013) (emphasis added). Dr. Hastings opines that the specification would not enable a POSA to practice the full scope of claim 1. *See, e.g.*, D.I. 604-6 (Hastings Suppl.) ¶¶ 183-217. In doing so, she necessarily must first address the claim scope, which includes antisense oligonucleotides with 5' and 3' end modifications. *Id.* at ¶¶ 55,

206, 207, 209. The specification states that such modifications fall within the scope of the invention. D.I. 2-9, Ex. I ('851 patent) at 27:47-59.

Sarepta seeks to exclude Dr. Hastings' opinions about enablement of 5' and 3' end modifications because "the claim does not recite any such modifications." D.I. 611 at 13. But in its very next breath Sarepta agrees with Dr. Hastings' claim interpretation: "to be sure, such modifications are ***not excluded*** from the claim." *Id.* Because such modifications fall within the scope of the genus claim, Dr. Hastings must consider whether Sarepta has enabled the ***full scope*** of the claim without undue experimentation. *Wyeth*, 720 F.3d at 1384.

Federal Circuit Judge Dyk's opinion for this Court while sitting by designation in *Baxalta Inc. v. Genentech, Inc.*, 579 F. Supp. 3d 595, 601 (D. Del. 2022), *aff'd*, 81 F.4th 1362 (Fed. Cir. 2023), is instructive. In *Baxalta* the claim was short: "An isolated antibody or antibody fragment thereof that binds Factor IX or Factor IXa and increases the procoagulant activity of Factor IXa." *Id.* In considering enablement, Judge Dyk focused on what the claim "covered," including "humanized and chimeric antibodies," "bispecific antibodies," as well as antibodies of various isotypes—none of which were specified by the claim language but all of which fell within the scope of the claim. *Id.* at 599; *see also id.* at 609 (considering the scope of what the claim "encompasses"). Judge Dyk explicitly rejected the patentee's argument that "the court should not be concerned with the lack of enablement of" a certain bispecific antibody that fell within the scope of the claim, regardless of whether it was named. *Id.* at 624.

Like the bispecific antibodies in *Baxalta*, Sarepta agrees a morpholino antisense oligonucleotide with 5' and 3' end modifications falls within the scope of claim 1. And, like the patentee in *Baxalta*, Sarepta asks the Court not to be concerned with the lack of enablement of that category of species. As in *Baxalta*, the Court should reject Sarepta's arguments. Dr. Hastings'

opinions regarding the end modifications that fall within the scope of the claims are plainly relevant to enablement. *See also Morphosys v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354, 368-369 (D. Del. 2019) ("the full scope of a claim is not enabled when there is an embodiment within the claim's scope that a person of ordinary skill, reading the specification, would be unable to practice without undue experimentation").

The cases on which Sarepta relies are either explicitly not on point or are so old as to predate modern enablement law. *United Therapeutics Corp. v. Liquidia Techs., Inc.*, 74 F.4th 1360, 1371 (Fed. Cir. 2023), involved a claim directed to a method of treatment, and the Federal Circuit characterized Liquidia's request to "analogiz[e] a subset of patients having a variant of a particular disease to traditional genus and species claims" as "inapt." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1545 (Fed. Cir. 1983), addressed processes for stretching thread seal tape, not broad genus claims. *W.L. Gore* also predates the Federal Circuit's 1988 decision in *Wands*, 858 F.2d at 731, and the Federal Court's more recent enablement precedent. Indeed, the Federal Circuit has not cited *W.L. Gore* when discussing enablement law for at least the past 20 years. *Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F. Supp. 1278, 1292 (D. Del. 1987)—which considered a patent application from 1953 directed to crystalline polypropylene—also predates *Wands*, and instead relied on *W.L. Gore*. Despite alleging the Federal Circuit has rejected Dr. Hastings' approach "time and again," D.I. 611 at 15, Sarepta fails to identify a single persuasive case supporting exclusion of Dr. Hastings' enablement opinions.

Finally, should the Court exclude any opinions from Dr. Hastings on enablement related to end cap modifications, any such exclusion would have to be narrow because Dr. Hastings' end cap modifications analysis is also relevant to her written description opinion, where she opines that the

scope of claim 1 far exceeds the disclosure in the specification. *See, e.g.*, D.I. 604-6 (Hastings Suppl.) ¶¶ 44, 55.

V. ARGUMENT IN RESPONSE TO MOTION #4

A. Dr. Hastings' Opinions Are Properly Based on an Objective Inquiry Into the Specification

Sarepta makes two arguments in Subsection A of its Motion #4. Neither warrant exclusion.

First, Sarepta argues that that extrinsic evidence is never relevant to the written description. D.I. 611 at 16. Sarepta is wrong. *See, e.g.*, *Immunex Corp. v. Sandoz Inc.*, 964 F.3d 1049, 1064 (Fed. Cir. 2020) (where district court considered extrinsic evidence, holding "Sandoz's argument that the district court erred by looking outside the four corners of the specification . . . is without merit"); *Biogen Int'l GmbH v. Mylan Pharm. Inc.*, 2020 WL 3317105, at *13 (N.D. W. Va. June 18, 2020), *aff'd*, 18 F.4th 1333 (Fed. Cir. 2021) (an entire subsection of the opinion is titled "Extrinsic Evidence Confirms the Lack of Written Description"). Instead, a proper analysis may include extrinsic evidence as long as the analysis is "[]tethered to" and draws a "basis in" the specification. *Allergan USA, Inc. v. MSN Laboratories Priv. Ltd.*, 111 F.4th 1358, 1376 (Fed. Cir. 2024).

Sarepta complains of Dr. Hastings' consideration of [redacted]. D.I. 604-6 (Hastings Suppl.) ¶¶ 134-135. But Dr. Hastings [redacted] while "[]tethered to" the specification, as she uses them only "to see whether they shed light on the interpretation or significance of the data in the UWA Patents." *Id.* Rather than relying on the [redacted] alone, she compares the data from [redacted] to the data in the patent. *Id.* at ¶¶ 146-147. This type of analysis is not

improper, and in considering [redacted] while basing her opinions on the specification, Dr. Hastings does not misapply the law.

Second, Sarepta accuses Dr. Hastings of engaging in a "subjective" rather than the required "objective" inquiry. Again, Sarepta is wrong. Sarepta mischaracterizes Dr. Hastings' testimony at D.I. 612, Ex. 3 (Hastings Suppl. Dep.) 39:13-41:20. Dr. Hastings never testified that **her analysis** was subjective; rather, she testified that a skilled artisan would did not trust the '851 patent's reference to "very faint skipping" as representing a meaningful result because a POSA would understand that the inventors' **characterization of "very faint"** is "subjective." *Id.* Dr. Hastings performs the requisite objective inquiry, and Sarepta's disingenuous argument to the contrary fails.

B. Dr. Hasting's Opinions on Therapeutic Efficacy and Evidence of Exon Skipping Are Not Improper

Sarepta's final legal challenge fares no better. Sarepta interprets the written description standard as creating a low bar and then accuses Dr. Hastings of applying a heightened standard by requiring written description of therapeutic levels of exon skipping. D.I. 611 at 18. But Sarepta does not dispute that claim 1 covers embodiments that achieve these results. *Id.* at 19 ("ASOs that induce therapeutic levels of exon skipping are included in the claim"). And, again, "the [written] description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented **what is claimed**." *Ariad Pharms.*, 598 F.3d at 1351 (emphasis added). Using this standard, Dr. Hastings properly opines that a POSA would not recognize the named inventors invented antisense oligonucleotides that achieve therapeutic levels of exon 53 skipping based on what is described in the specification, and there is no written description. D.I. 604-6 at ¶¶ 126, 133, 153, 155, 182. Once again, Sarepta is simply wrong on the law. Indeed, Sarepta fails to cite

a single case where expert opinion on this topic was deemed improper or irrelevant to written description.[2] NS knows of none, and such a ruling would be contrary to Federal Circuit precedent.

In *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1343-44 (Fed. Cir. 2005), the patent-at-issue recited a method for "selectively viewing areas of an image at multiple resolutions" that included forming and using a "seamless" discrete wavelet transform. The specification provided only one method for creating a seamless discrete wavelet transform, but the claim was directed to creating any seamless array of discrete wavelet transform coefficients. *Id.* The Federal Circuit held that the claim lacked written description support. *Id*. at 1346-67. The Federal Circuit warned against interpreting written description in a way that "would lead to sweeping, overbroad claims because it would entitle an inventor to a claim scope far greater than what a person of skill in the art would understand the inventor to possess." *Id.* "Thus, a patentee cannot always satisfy the requirements of section 112, in supporting expansive claim language, merely by clearly describing one embodiment of the thing claimed." *Id.*

Similarly, in *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330, 1337 (Fed. Cir. 2021), the Federal Circuit held "[t]he disclosure of one scFv that binds to CD19 and one scFv that binds to a PSMA antigen on prostate cancer cells in the manner provided in this patent does not provide information sufficient to establish that a skilled artisan would understand how to identify the species of scFvs capable of binding to the limitless number of targets as the claims require." And in *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300–01 (Fed. Cir. 2014), the Federal Circuit affirmed a verdict of invalidity for lack of written description because the patent disclosed only one very limited subgenus within a diverse claimed genus.

[2] The only case Sarepta cites, *In re Brana*, 51 F.3d 1560, 1564 (Fed. Cir. 1995), is almost 30 years old and addresses utility.

Here, as Sarepta's own expert admits, Sarepta's claim 1 covers all levels of exon 53 skipping, from "very faint" to complete. D.I. 604-10 (Dowdy Suppl. Dep.) 314:2-315:17. Yet the specification at most discloses a species that shows "very faint" exon 53 skipping. D.I. 2-9, Ex. I ('851 Patent) Table 39; *see also* D.I. 604-6 (Hastings Suppl.) ¶ 86. Dr. Hastings opines that this disclosure of at most one embodiment does not provide information sufficient to establish that a POSA would understand the entire scope of the claims. *See* D.I. 604-6 at ¶¶ 33-144. Dr. Hastings' opinions are admissible, as she is applying the standard that draws directly from Federal Circuit precedent.

Continuing to fight an unwinnable battle, Sarepta asserts "if the '851 Patent inventors had described their exon skipping data prophetically, that would be sufficient." D.I. 611 at 20. While "[p]rophetic examples . . . certainly can be sufficient to satisfy the written description requirement." a disclosure that "is not so much an 'example' as it is a mere mention of a desired outcome" of therapeutically effective exon 53 skipping cannot. *Ariad Pharm., Inc.*, 598 F.3d at 1357; *see also Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 918, 923 (Fed. Cir. 2004) (patent claims directed to COX–2 inhibitors were invalidated for lack of adequate written description because the existence of such inhibitors was merely "hypothesized"; no such inhibitors were yet known and none were described in the patent).

In short, the Federal Circuit's cases show "show that patent claims may be invalidated based on the failure to disclose any, or more than one, species in a nascent area where knowledge of the art has nothing to add to the disclosure." *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 649 (E.D. Tex. 2017), *aff'd*, 739 Fed. Appx. 643 (Fed. Cir. 2018). Here Dr. Hastings points to plenty of record evidence demonstrating the field was highly unpredictable,

such that "knowledge of the art has nothing to add to the disclosure." *Id.*; *see* D.I. 604-6 (Hasting Suppl.) ¶¶ 186-196.[3]

Sarepta may disagree with Dr. Hastings' opinions, but it can cross examine her on them. Sarepta has not identified a single basis for exclusion. Motion #4 should be denied.

VI. CONCLUSION

For the foregoing reasons, NS respectfully requests the Court deny Sarepta's four *Daubert* motions.

[3] Sarepta mischaracterizes [redacted] D.I. 611 at 20 n.9. But Dr. Hastings expressly noted [redacted]. D.I. 604-6 (Hastings Suppl.) ¶ 162.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

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